

**RECEIVED
CENTRAL FAX CENTER****OCT 16 2007**U.S. Serial No. 10/723,795
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Page 1 of 13AMENDMENTS TO THE CLAIMS

Claims 1-66 (canceled).

Claim 67 (previously presented): A method that is diagnostic or diagnostic and prognostic for precancer or cancer comprising contacting a mammalian sample with a potent MN/CA IX-specific inhibitor conjugated to a label or a visualizing means, and detecting or detecting and quantifying binding of said potent MN/CA IX-specific inhibitor to MN/CA IX on cells in said sample by detecting or detecting and quantifying said label or said visualizing means on cells in said sample, wherein said detection or said detection and quantitation at a level above that for a control sample is indicative of precancerous or cancerous cells that overexpress MN/CA IX in said sample;

wherein said inhibitor is selected from the group consisting of organic heterocyclic and aromatic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_i of said compound;

wherein if said inhibition constant K_i is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

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wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of each of the carbonic anhydrases in the group consisting of CA I, CA II and CA IV.

Claim 68 (previously presented): The method of claim 67 wherein MN/CA IX is detected or detected and quantitated, and the mammal from whom the sample was taken is considered to have a poor prognosis, and decisions on treatment for said mammal are made in view of the level of said MN/CA IX.

Claim 69 (previously presented): A method for imaging tumors and/or metastases that express MN/CA IX in a patient comprising the administration of a potent MN/CA IX-specific inhibitor linked to an imaging agent to said patient;

wherein said inhibitor is selected from the group consisting of heterocyclic and aromatic organic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_i of said compound;

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wherein if said inhibition constant K_i is determined to be less than about 50 nanomolar, said inhibitor is determined be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of each of the carbonic anhydrases in the group consisting of CA I, CA II and CA IV.

Claim 70 (currently amended): A diagnostic/prognostic method for a preneoplastic/neoplastic disease associated with abnormal MN/CA IX expression, comprising detecting or detecting and quantifying MN/CA IX in a vertebrate sample, comprising:

a) contacting said sample with a cell membrane-impermeant, potent specific inhibitor of MN/CA IX conjugated to a label or a visualizing means, and

b) detecting or detecting and quantifying binding of said specific inhibitor of MN/CA IX in said sample by detecting or detecting and quantifying said label or said visualizing means on cells in said sample, wherein said detecting or said detecting and quantifying at a level above that for a control sample is indicative of precancerous or cancerous cells that abnormally express MN/CA IX in said sample;

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wherein said inhibitor is selected from the group consisting of cell membrane-impermeant heterocyclic and aromatic organic compounds, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_i of said inhibitor;

wherein if said inhibition constant K_i is determined to be less than about 50 nanomolar, said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of CA IV.

Claim 71 (canceled).

Claim 72 (previously presented): The method of claim 70 wherein said cell membrane-impermeant MN/CA IX-specific inhibitor is an MN/CA IX-specific aromatic or heterocyclic sulfonamide.

Claim 73 (previously presented): The method of claim 72 wherein said MN/CA IX-specific aromatic or heterocyclic

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sulfonamide is a cell membrane-impermeant pyridinium derivative of an aromatic or heterocyclic sulfonamide.

Claim 74 (previously presented): The method of claim 72 wherein said MN/CA IX-specific aromatic or heterocyclic sulfonamide is selected from the group consisting of Compounds 1-91.

Claim 75 (previously presented): The method of claim 72 wherein said MN/CA IX-specific sulfonamide is selected from the group consisting of Compounds 1-26 .

Claim 76 (canceled).

Claim 77 (currently amended): The method of claim [[76]] 70, wherein said label is fluorescein isothiocyanate.

Claim 78 (currently amended): The method of claim [[76]] 70, wherein said method is used as an aid in selection of patient therapy.

Claim 79 (previously presented): The method of claim 78, wherein said binding to MN/CA IX is detectable at a level

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above that for a control sample, and said method is used in the decision to use MN/CA IX-targeted therapy.

Claim 80 (previously presented): The method of claim 78, wherein said therapy comprises the use of MN/CA IX-specific inhibitors, conventional anticancer drugs, chemotherapeutic agents, different inhibitors of cancer-related pathways, bio-reductive drugs, radiotherapy, MN/CA IX-specific antibodies and MN/CA IX-specific antibody fragments that are biologically active.

Claim 81 (currently amended): The method of claim [[76]] 70, wherein said method is used to monitor the status of a cancer patient.

Claim 82 (previously presented): The method of claim 81, wherein said method is used to monitor cancer chemotherapy and tumor reappearance, detect the presence of cancer metastasis, and/or confirm the absence or removal of all tumor tissue following surgery, cancer chemotherapy and/or radiation therapy.

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Claim 83 (previously presented): A method of imaging a tumor or tumors and/or metastases that express MN/CA IX in a patient, comprising:

- a) administering to said patient a cell membrane-impermeant, potent specific inhibitor of MN/CA IX, said inhibitor linked to an imaging agent; and
- b) detecting the binding of said inhibitor;

wherein said inhibitor is selected from the group consisting of cell membrane-impermeant heterocyclic and aromatic sulfonamides, and wherein said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity in a screening assay comprising determining the inhibition constant K_i of said inhibitor, wherein if said inhibition constant K_i is determined to be less than about 50 nanomolar, said inhibitor is determined to be a potent inhibitor of MN/CA IX enzymatic activity; and

wherein said potent inhibitor is determined to be an MN/CA IX-specific inhibitor if it is a more potent inhibitor of MN/CA IX enzymatic activity than of the enzymatic activity of CA IV.

Claim 84 (previously presented): The method of claim 83 wherein said specific inhibitor of MN/CA IX is positively-

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charged, membrane-impermeant aromatic or heterocyclic sulfonamide.

Claim 85 (previously presented): The method of claim 84 wherein said membrane-impermeant sulfonamide is a pyridinium derivative of an aromatic or heterocyclic sulfonamide.

Claim 86 (previously presented): The method of claim 72 wherein said MN/CA IX-specific sulfonamide is selected from the group consisting of Compounds 27-70.

Claim 87 (previously presented): The method of claim 67 wherein said group consisting of organic heterocyclic and aromatic compounds is a group consisting of heterocyclic and aromatic sulfonamides.

Claim 88 (previously presented): The method of claim 87 wherein said group consists of Compounds 1-91.

Claim 89 (previously presented): The method of claim 69 wherein said group consisting of organic heterocyclic and aromatic compounds is a group consisting of heterocyclic and aromatic sulfonamides.

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Claim 90 (previously presented): The method of claim
89 wherein said group consists of Compounds 1-91.